Remarks

Applicants would like to thank the Examiner for considering the remarks made in the previous response by Applicants and have rejoined inventions I and II. The Examiner's objections have been rectified with entry of the above amendment to the claims. No new matter has been added by these amendments.

Rejection of claim 19 under 35 USC §101

Claim 19 has been canceled; hence the rejection made under this section is moot.

Rejection of claims 1-21 under 35 USC §112, second paragraph

Claims 1, 3-18 and 21 have been amended according the rejection made under this section. Claims 2, 19 and 22 have been canceled. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections under 35 §USC 102(b)

Claims 1, 3-6 8-10 and 15-17 are rejected under 35 §USC 102(b) as being anticipated by Fellenberg et al as evidenced by de Almeida et al. Withdrawal of this rejection is respectfully requested.

Fellenberg et al is teaches transgenic yeast containing a heterologous CDC14 gene that is overexpressed in said yeast. While not taught by Fellenberg et al, the Examiner states that the reference teaches phenotyping the organism because it was known in the art at the time of the Fellenberg publication that overexpression of CDC14 causes cell cycle arrest. The Examiner puts forth the de Almeida et al reference as evidence to this point.

Claim 1 and dependent claims therefrom have been amended to state the phenotyping is carried out by measuring the reduction or elimination of compensating differential expression or by labeling at least one compensating differentially regulated gene. As such, Applicants submit that Fellenberg et al either alone or in combination with de Almeida does not anticipate the claimed invention since there is no teaching or suggestion in Fellenberg et al for phenotyping a modified organism as taught by Applicants. Accordingly, Applicants believe that the rejection has been overcome and withdrawal of the rejection is respectfully requested.

Claims 1, 3-6, 8, 10 and 16-17 are rejected under 35 §USC 102(b) as being anticipated by Suzuki et al. Applicants traverse the rejection.

Applicants amended claim 1 and dependent claims therefrom such that the phenotyping is carried out by the reduction or elimination of compensating differential expression or by the labeling of at least one compensating differentially regulated gene which is not taught by Suzuki et al. Furthermore, the claims recite a method for generating a **"genetically modified organism"**. On page 1, lines 33-38 of the specification, Applicants define a "genetically modified organism" as an alteration that can be perceived or measured from the outside of the organism such as shape, size, growth, rate of division, etc. Suzuki et al requires the use of a microarray assay to measure the internal increase or decrease of gene expression. Applicants submit that Suzuki et al does not anticipate the claimed invention and that the rejection should be withdrawn.

Claims 1-8, 11-14 and 17-18 are rejected under 35 §USC 102(b) as being anticipated by Rohlmann et al as evidenced by Ishibashi et al.

Rohlmann et al teaches a double knockout mouse comprising a homozygous disruption of LRP and LDLR which exhibit defective remnant removal. The Examiner states that the phenotype of the knockout mouse is the up-regulation of the LDL receptor. This differs from the claimed genetically modified organism wherein the modification must be perceived or measured from the outside of the organism as defined in the application on page 1, lines 33-38, for example. The claimed methods also recite that the method is to generate a **genetically modified organism** for drug screening which requires phenotyping the organism as defined by the Applicants in the specification to only be an externally perceptible phenotype. As such it is submitted that Rohlmann does not anticipate the claimed invention. Withdrawal of this rejection is respectfully requested.

Claims 1, 3, 5-9, 15, 17, and 19-21 are rejected under 35 §USC 102(b) as being anticipated by Tugendreich et al. This rejection is respectfully traversed.

Tugendreich et al does not teach a method for generating a genetically modified organism wherein as one of the methods steps the phenotyping is carried out by the reduction or elimination of compensating differential expression or by the labeling of at least one compensating differentially regulated genes. It is submitted that since Tugendreich et al does not anticipate the amended claims, the rejection is overcome. Withdrawal of this rejection is respectfully submitted.

Rejections under 35 §USC 103(a)

Claims 19-21 are rejected under 35 §USC 103(a) as being unpatentable over Rohlmann et al in view of Capecchi.

Rohlmann is cited for teaching a double knock-out mouse that has higher cholesterol and triglyceride levels than control mice. As admitted by the Examiner, Rohlmann does not teach using their animal system in a screening assay for substances having an effect on the function of a heterologous protein or protein fragment. The secondary reference of Capecchi is applied as fulfilling that deficiency. Applicants respectfully submit that Capecchi does not provide a teaching or suggestion to use a knock-out mouse as taught by Rohlmann for screening substances that would have an effect on the function of a heterologous expressed protein or protein fragment. It is agreed that knock-out mice are useful in analyzing pathology of diseases and as vehicles for exploring new therapies such as gene therapy but it is well understood in the field that knock-out mice are not a source for primary cell assays for drug screens. As such, it is submitted that the combination of references cited above does not teach or suggest the claimed invention. Withdrawal of this rejection is respectfully requested.

Claims 19-21 are rejected under 35 §USC 103(a) as being unpatentable over Fellenberg et al in view of Tugendreich et al. Fellenberg et al is cited for the teaching of the identification of genes in yeast cells upon CDC14 induction but lacking in a teaching of using such cells in a screening assay for agents that affect CDC14. The secondary reference of Tugendreich is cited for teaching the widespread recognition of cell-based assays using organisms such as yeast for screening rapidly.

Applicants submit that the combination of references does not teach or suggest the claimed invention for the following reason. Fellenberg et al is deficient in teaching or suggesting methods of using transgenic yeast cells that overexpress CDC14 in drug screening assay to measure substances and also does not teach or suggest transgenic organism having a genetically modified phenotype caused by the reduction or elimination of a compensating differential gene. Nor does Tugendreich et al teach or suggest using genetically modified organisms in screening assays to measure the effect of substances on such genetically modified organisms as compared to genetically unmodified organisms. Applicants submit that the combination of Fellenberg et al with Tugendreich et al would not result in or suggest the claimed invention. Withdrawal of this rejection is respectfully submitted.

Should the Examiner believe that an interview would advance the prosecution of this application, the Applicants invite him to contact the undersigned at 908.231.4658.

Respectfully submitted,

Karen I. Krupen, Reg. No. 34,647
Attorney for Applicants

sanofi-aventis
Patent Department
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807-0800
Telephone (908) 231-4658
Telefax (908) 231-2626
Aventis Docket No. DEAV2002/0089 US NP